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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,627	03/06/2002	Dan Yang	609920-600-025	1956

7590 09/16/2003

Stephen D. Scanlon
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North Point
901 Lakeside Avenue
Cleveland, OH 44114

EXAMINER

BADIO, BARBARA P

ART UNIT	PAPER NUMBER
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1616

DATE MAILED: 09/16/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

10/091,627

Applicant(s)

YANG ET AL.

Examiner

Barbara P. Badio, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-63 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-63 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-946) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>8</u> . | 6) <input type="checkbox"/> Other: |

Final Office Action on the Merits

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

2. The rejection of claims 1-63 under 35 USC 112, second paragraph is withdrawn.

3. The rejection of claims 1-63 under 35 USC 103(a) over Bovicelli et al., Cicala et al., Holland et al. and Yang et al. (J. Org. Chem., 1998 or US Patent No. 5,763,623) in combination is maintained.

Applicant argues that it is immaterial whether it would have been obvious to use a dioxirane derivative in the epoxidation of olefinic compounds or whether there was a reasonable expectation that any 5-ene steroid derivation would undergo epoxidation with the production of the corresponding 5,6-epoxy compounds or that dioxirane derivatives would be produced in situ by the reaction of a ketone and an oxidant. According to applicant, none of these factors goes to the selection of particular steroids and/or particular ketones or dioxiranes to achieve epoxides of a desired stereoselectivity. Applicant's argument was considered but not persuasive for the following reasons.

First, it is noted that applicant argues each reference individually. However, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Second, the examiner disagrees that the teachings of the prior art are immaterial because they do not teach the selection of particular steroids and/or particular ketones or dioxirane to achieve epoxides of a desired stereoselectivity. The teachings of the prior art are material to what was known by the ordinary artisan in the art at the time of the present invention and, thus, what the skilled artisan would expect based on said teachings and the level of skilled of the ordinary artisan. The issue is not whether the prior art teaches the selection of particular substrates and reactants but whether the prior art makes obvious said combination/selection.

The cited prior art teach (a) the production of mostly 5 β ,6 β -epoxides of steroids from the corresponding 5-ene steroids using dioxiranes (see Bovicelli and Cicala); (b) the in situ production of dioxiranes by reaction of a ketone, including those of the instant claims, and an oxidizing agent and (c) the epoxidation of 5-ene-3 α -substituted steroids in the presence of an oxidant. Based on these teachings and the level of skill of the ordinary artisan in the chemical art at the time of the invention, it is the examiner's position that the epoxidation of 5-ene steroids using an oxidant such as dioxiranes, including those produced in situ by the reaction of a ketone, such as those of the instant claims, and an oxidizing agent would have been obvious to the skilled artisan in the art

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at the time of the present invention. The question of the production of mostly the $5\beta,6\beta$ -epoxides would be prima facie obvious because both Bovicelli and Cicala teach that epoxidation of 5-ene steroids in the presence of a dioxirane result in the production of mostly the corresponding $5\beta,6\beta$ steroid derivatives. In addition, it is within the level of skill of the ordinary artisan to determine the optimum reaction condition necessary to increase the yield of the $5\beta,6\beta$ -epoxide steroid from the corresponding 5-ene steroid in the presence of a dioxirane. The examiner notes that both Bovicelli and Cicala exemplify a 3β -substituted steroid. However, epoxidation of 3α -substituted steroid in the presence of an oxidant is known in the art and, thus, based on the teachings of the cited prior art, the skilled artisan would have the reasonable expectation that said 3α -steroid derivative would undergo epoxidation in the presence of a dioxirane with the production of the corresponding $5\beta,6\beta$ -epoxide.

The examiner notes applicant's argument that the ratio taught by Bovicelli does not compare favorably with the ratios reported in the present application and that the reference does not teach the specific dioxiranes, namely those of formulae VII, VIII, IX and X, would yield a substantially higher β/α -epoxides when used in the epoxidation of 3α -steroids. In response to applicant's argument, it is noted that the dioxirane exemplified by Bovicelli is encompassed by the claimed dioxiranes of formula IX and that based on the teachings of the cited prior art, epoxidation of any 5ene steroid, including the 3α -derivatives, would be prima facie obvious.

In summary, based on the combined teachings of the references cited above, it is obvious that (a) dioxiranes are useful oxidants; (b) 5-ene steroids undergo epoxidation

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in the presence of an oxidant and (c) the epoxidation of 5-ene steroids in the presence of a dioxirane results in the production of mostly the corresponding 5 β ,6 β -epoxide derivative. The skilled artisan would have the reasonable expectation that any dioxirane would be useful in the epoxidation of any 5-ene steroid with the production of mostly the 5 β ,6 β -epoxides. It would also be obvious to the skilled artisan in the chemical art that increase in the yield of the end product can be obtained by changes in the reaction conditions. The determination of said reaction conditions is within the level of skill of the ordinary artisan.

For these reasons and those given in Paper No. 6, the rejection of claims 1-63 under 35 USC 103(a) over Bovicelli et al., Cicala et al., Holland et al. and Yang et al. (J. Org. Chem., 1998 or US Patent No. 5,763,623) in combination is maintained.

Other Matters

4. The examiner requests correction of the structures in claims 15, 27, 37, 42 and 53 (see formulae II, I, XII and XIV in the above mentioned claims).

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

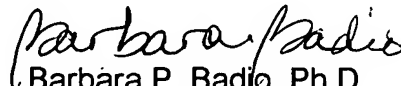
6.

Telephone Inquiry

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio, Ph.D. whose telephone number is 703-308-4595. The examiner can normally be reached on M-F from 7:30am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308- 2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


Barbara P. Badio, Ph.D.
Primary Examiner
Art Unit 1616

BB
September 15, 2003